
Appendix B

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Hygroscopic Cervical Dilators: A literature Review

Abstract: Hygroscopic cervical dilators have been successfully used by physicians for over 150 years. Synthetic alternatives to the naturally occurring Laminaria were introduced in the early 80's and have been found to be a safe and effective alternative to Laminaria. This review presents a summary of medical literature pertaining to the safety, efficacy and mechanism of action of cervical dilators with a focus on Lamicel.

Doctors have successfully used hygroscopic cervical dilators for over 150 years. Until 1982, laminaria, which is made from the root of seaweed, was the only available hygroscopic cervical dilator. Laminaria works by expanding and thereby dilating the cervix when inserted in the cervical os. This natural dilator became associated with sterility concerns which peaked interest in the creation of a synthetic hygroscopic cervical dilator (Johnson 1990). Synthetic dilators replicate the action of laminaria but avoid the complications and irregularity of a naturally occurring product. This review presents a summary of the medical literature from 1982 to 2004, with particular reference to the reported safety and efficacy of synthetic dilators versus the natural alternative, laminaria.

Background on Rational for Synthetic Dilators

Currently there are only 2 synthetic dilators available on the US market, Dilapan-S (JCEC Co) and Lamicel (Medtronic Xomed). These synthetic alternatives to laminaria offer the potential advantages of assured sterility, consistency of shape and length, and in theory a greater predictability of effect (Lichtenberg 2004).

The natural origin of laminaria has created concern surrounding its predictability and sterility. A 1989 review by Nicholas Johnson listed the following reported complications with natural tents (Johnson 1989):

“migration of the tent into the cavity, tent expulsion, fracture and fragmentation of the tents occurring during tent removal leaving pieces of seaweed within the canal and uterine cavity, disintegration of entire batches of Laminaria have been recorded and the literature contains cases of tents creating false passages, reports of tents causing inadvertent rupture of the amniotic membranes and a single report of fetal death occurring in association with Laminaria”

In an effort to overcome these complications, advocates have promoted the use of synthetic dilators. Potential benefits include; uniformity of size and shape, uniformity of dilatation characteristics, assurance of sterility, reduced expense, ability to control the rate and amount of dilation, and ability to control the shape of the device (Brenner 1982).

Despite the complications reported by Johnson, laminaria tents are still accepted as safe and effective for cervical dilation. The overwhelming concern surrounding laminaria is based on historical experiences with sepsis resulting from improperly sterilized product. While sterilization processes have improved, laminaria still contains the potential risk of seaweed spores that are resistant to the sterilization process (Wells 1989) a risk avoided by the synthetic cervical dilators.

Efficacy of Synthetic Cervical Dilators

Lamicel and Dilapan were both designed to mimic the effect of laminaria. Dilapan is a synthetic tent derived from hypan which swells to 3 times its size within an hour when placed in water. Lamicel is an alternative synthetic tent that uses a sponge pretreated with magnesium sulfate to expand the cervix. In a study published in 1983, Wheeler and Scheider concluded that Lamicel was as effective as its natural counterpart laminaria. In addition, due to the reduced pressure Lamicel applies to the cervix they found it to be the safest method of cervical dilation available (Wheeler 1983).

Both Lamicel and Dilapan have been found to be at least as effective as laminaria. A 1988 comparative study of 100 patients using Lamicel or laminaria for mid-trimester termination of pregnancy found the degree of cervical dilation achieved with Lamicel to be significantly greater than that achieved by laminaria. In addition, Lamicel was successful in pregnancy termination in all 50 patients, while laminaria was only effective in 43 out of 50, a success rate of only 86%. In a 1989 review, Johnson cites Dilapan as being superior to Lamicel in the final dilation and speed of action. However, Dilapan harbors the risk of fracture and fragment similar to that of laminaria (Johnson N 1989). There are no reports of Lamicel fracturing.

Complications with Cervical Dilators

A 2004 review by E. Steve Lichtenberg reviewed complications associated with hygroscopic dilators. Through his literature review of articles from 1972 to 1999 Lichtenberg noted 47 reported mechanical complications. These results are shown in Table 1. Of the complications reported the most common problem was fragmentation of the dilator. Lichtenberg notes that all listed cases of fragmentation resulted in benign outcomes. The 1996 case of a patient reporting a 10-year history of pelvic pain and bleeding is the only reported case, where a patient retained a nearly entire Dilapan device. The patient reported pain 10 years after an apparently uneventful abortion at 20 weeks gestation. Lichtenberg postulates that newer radiographic techniques could be helpful in identifying such retained dilators.

In addition to mechanical complications, Lichtenberg noted two additional risks of infection and two cases of anaphylaxis. Reports of infection attributed solely to osmotic devices were uncommon. Instead, most infections arose from retained tissue or uterine injury. Supporting his claim is a first-trimester randomized trial of 519 patients comparing patients pretreated with laminaria with a control group. This trial showed patients pre-treated with a single laminaria tent had a lower rate of post-abortion infection than the control group. There has been one reported case of toxic shock syndrome associated with cervical tents were laminaria

was used. No trials in the past 20 years have reported infection as a troublesome complication attributed to the use of cervical tents.

Table 1: Mechanical complications with hygroscopic dilators			
From: Lichtenberg, E.S.,2004			
Year published	Number of patients	Type of dilator	Problem
1972	3	Laminaria	Impaction
1973	3	Laminaria	Impaction
1975	2	Laminaria	Impaction, fragmentation and endometritis
1983	1	Laminaria	Impaction and displacement
1991	1	Laminaria	Impaction, fragmentation and displacement
1994	1001	Laminaria and Dilapan	Impaction: Laminaria 1/498 (.2%) Dilapan 9/505 (1%) Fragmentation: Laminaria 0/496 (0%) Dilapan 22/505 (4%)
1996	1	Laminaria	Missing laminaria
1996	1	Laminaria	Possible incomplete laminaria tent
1996	1	Dilapan	10-year history of pelvic pain and bleeding

Lichtenburg's review article found 2 cases of nonfatal anaphylaxis to laminaria. Anaphylaxis arises from an allergic reaction to the natural components of seaweed. No such cases have been attributed to synthetic devices.

Safety Across Markets

While only approved in the US for cervical dilation for hysteroscopy or termination of pregnancy, cervical tents have been studied for their ability to dilate the cervix for a variety of procedures. In 1990 Berkus et al. studied the use of Lamicel for induction of labor. Berkus found Lamicel to be safer than laminaria resulting in a similar success rate, but lower maternal infection, neonatal sepsis, and no mortality (Berkus 1990). Similar studies have been conducted by Grimes et al. and Bagratte both of who found Lamicel to be a safe and effective alternative for inducing labor (Grimes 1987) (Bagratte 1990).

Mechanism of Action

Nicholas Johnson found through his 1989 review of intracervical tents that the precise mechanism of action of both natural and synthetic tents is unknown. Dilapan and laminaria both act by a combination of forceful expansion and local changes in prostaglandin biochemistry. Lamicel on the other hand has been found to provide an insufficient radial force to expand the cervix (Wheeler 1983).

While the mode of action has been of great discussion, our search of the literature found synthetic cervical dilators to be equally effective to laminaria without the inherent risks of the

naturally occurring product. Both Dilapan and Lamicel were found to be more predictable in their expansion and safer in their risk of non-sterility than laminaria.

Nicolaides et al. studied Lamicel for cervical dilatation before first trimester abortion. During this study Nicolaides achieved successful insertion of Lamicel in 90% of his patients. Insertion of Lamicel was attempted unsuccessfully in 2 patients. In the unsuccessful cases, Lamicel was left proximal to the cervical os and dilation still occurred. This led the authors to the conclusion that Lamicel's effects were not entirely mechanical (Nicolaides 1983).

A separate study in Sweden compared the effect of Lamicel versus the same synthetic sponge without the magnesium salt addition. In this study, 87 healthy and pregnant patients were admitted to the hospital for a first trimester abortion. Forty-five patients were randomly assigned to be pretreated with either a Lamicel tent or a similar tent that had not been pretreated with $MgSO_4$. Forty-two patients were selected as controls to receive no pre-treatment. The authors found that Lamicel pre-treatment before vacuum aspiration created a more favorable cervix when compared to the control group. However, they found the synthetic tents without $MgSO_4$ to be equally efficient at dilating the cervix when compared to Lamicel. Their findings indicate Lamicel works through a mechanical effect vs a combination chemical and mechanical effect (Radestad 1989).

Again, while the exact mechanism of action for the various cervical tents is not fully understood, it should be noted that a study in Sweden found natural laminaria to be interchangeable with Lamicel. A study published in 1994 by Bokstrom reviewed combination treatments for second trimester abortions. Bokstrom noted that there were no differences between the Laminaria/Lamicel treatments with respect to the induction-abortion interval (Bokstrom 1995).

Safety of Lamicel versus Laminaria

A study published by Grimes et al. in 1987 also found Lamicel to be as safe and effective as laminaria. The measured outcomes are shown in Table 2.

Table 2: Selected Outcome Measures by Treatment Group		
From: Grimes et al 1987		
Outcome measure	Rate for Lamicel (per 100 abortions)	Rate for Laminaria (per 100 abortions)
Vasovagal reaction		
During insertion	0.9	4.5
After insertion	8.3	9.1
Bleeding upon removal	8.3	30.0
Initial dilation ≥ 37 French units	47.7	47.3
Ability to dilate to 43 French units	95.4	95.5
Cervical injury	2.8	0.0

As shown, the removal of Lamicel was associated with significantly less bleeding than the removal of laminaria, however no delayed complications or hospitalizations were reported in either group. Grimes notes that the “superficial” cervical injury which occurred in the three patients who received Lamicel was a nonsignificant difference to those who received laminaria. Grimes also noted the difference in cost for a cervical dilation was significantly less for the Lamicel group than for the laminaria group. This cost difference is based upon the use of a single Lamicel per procedure versus multiple laminaria (Grimes 1987).

Conclusions

A review of the literature from 1982-2004 has revealed the safety and efficacy of synthetic hygroscopic cervical dilators meets or exceeds that of their naturally occurring counter parts. A thorough search of the literature reveals that there have been no significant safety issues with the synthetic hygroscopic cervical dilator. While modern sterilization techniques have all but removed the risk of sepsis when using natural laminaria, the synthetic alternatives avoid this historical black mark. The most recent review article, which was published by Lichtenburg in 2004, found that hygroscopic cervical dilators offer protection from mild and serious cervical injuries and a reduction in the risk of uterine perforation during abortion. He noted Lamicel offered the increased safety characteristic of exerting no outward pressure on the cervical wall. Thus, the more recent clinical studies confirm that synthetic hygroscopic cervical dilators are at least comparable, and perhaps superior to their conventional counterparts.

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